REMARKS

Claims 1, 6-8 and 11 are pending. Claims 2-5, 9-10 and 12-28 are canceled. No new matter has been added.

Claim rejections – 35 U.S.C. §103

Claims 1, 6-7 and 8 are rejected under 35 U.S.C. §103(a) as obvious in view of Holden *et al.* (Am J Obstet Gynecol. 1998; 178(3):551-6) in combination with Ellis *et al.* (Acta. Obstr. Gynecol. Scand. 2001: 80, 602-608) and Boger (WO 2002/14873).

Claim 1 requires measuring asymmetric dimethylarginine (ADMA) in a plasma sample taken from a pregnant woman at a stage of pregnancy from 23 to 25 weeks gestation, and determining that the woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of ADMA in the plasma sample is greater than 1.5 µmol/L.

Holden describes ADMA levels of pre-eclamptic patients during only the third trimester. The third trimester is outside of the 23-25 week limitation of claim 1, therefore Holden does not disclose this limitation. Moreover, Holden's disclosure of an ADMA level of 1.17 µmol/L in the third trimester does not satisfy the claimed level of 1.5 µmol/L in the claimed stage of pregnancy of 23-25 weeks. That is, a measurement 1.17 µmol/L at 23-25 weeks would not trigger a determination that a woman is at risk of developing pre-eclampsia or that her fetus is at risk of developing IUGR.

Ellis describes measuring levels of dimethylarginines (including ADMA) and cytokines in mild and severe preeclamptic patients. Ellis describes testing patients to determine ADMA levels at a stage of pregnancy of 24-32 weeks. The range of ADMA levels of preeclamptic patients was determined to be in the range of 0.40-1.00 µmol/L. Thus, Ellis does not disclose an ADMA level of greater than 1.5 µmol/L. In fact, the levels observed by Ellis are lower than the level of 1.17 µmol/L observed by Holden.

Boger makes no mention of measuring any level of plasma ADMA in pregnant women during any stage of pregnancy, let alone a level of 1.5 μmol/L or greater at a stage of pregnancy from 23 to 25 weeks.

For a proper *prima facie* case of obviousness to be made, the combination of references must teach or suggest all claim limitations. None of the references suggests that a level of 1.5 μmol/L or greater at a stage of pregnancy from 23 to 25 weeks would be indicative of preeclampsia. Thus, the combination of Holden, Ellis and Boger fails to disclose or suggest measuring ADMA in a plasma sample taken from a pregnant woman at a stage of pregnancy from 23 to 25 weeks gestation, and determining that a woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of ADMA in a plasma sample is greater than 1.5 μmol/L, as required by claim 1. Therefore, none of the references teaches or suggests all of the claim limitations, and in addition the combination of references fails to teach or suggest all of the claim limitations.

Applicants respectfully request that this rejection be withdrawn.

Claims 1 and 11 are rejected under 35 U.S.C. §103(a) as obvious in view of Holden in combination with Ellis, Boger, and Albaiges *et al.* (Obstet. Gynecol. 2000; 96:559-64).

As described above, the combination of Holden, Ellis and Boger fails to disclose or suggest all of the limitations of claim 1. Albaiges fails to remedy this deficiency, as Albaiges also fails to disclose or suggest measuring ADMA in a plasma sample taken from a pregnant woman at a stage of pregnancy from 23 to 25 weeks gestation, and determining that a woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of

ADMA in a plasma sample is greater than 1.5 μmol/L.

Applicants respectfully request that this rejection be withdrawn.

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Respectfully submitted,

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